

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: William J. Curatolo et al.)
SERIAL NO.: 09/770,562) Examiner: B. Fubara
FILED: January 26, 2001) Art Unit: 1618
FOR: Solid Pharmaceutical Dispersions)
with Enhanced Bioavailability)
)

Commissioner for Patents
Washington, D.C. 20231

Sir:

DECLARATION UNDER 37 CFR 1.131

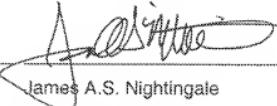
I, James A.S. Nightingale, declare that:

1. I was awarded the degree of Bachelor of Science in Chemical Engineering in 1980 by the University of Washington, Seattle, Washington, a degree of Master of Science in 1986 in Bioengineering by the University of Washington, Seattle, Washington, and a Ph.D. in 1988 in Bioengineering by the University of Washington, Seattle, Washington.
2. Prior to being employed with Bend Research I was employed from 1988-1993 as a Staff Scientist by Ciba-Geigy Corporation, Pharmaceuticals Division, Ardsley, New York where my areas of expertise included transdermal drug-delivery research and the development of second-generation transdermal pharmaceutical products; and from 1980-1988 as a Research Assistant for the University of Washington, Seattle, Washington, where my areas of emphasis included biomaterials, polymer synthesis and characterization, organic chemistry, biochemistry, and chemical engineering.

3. I have been employed by Bend Research, Inc., of which I am also a part owner since 1993. My title is Director, Pharmaceutical Research.
4. Bend Research, Inc. is part-owned by Pfizer, Inc., the Assignee of the above-identified application.
5. I am an inventor of the instant patent application.
6. I have reviewed the examples in the instant application. In particular attached to this declaration as Exhibit A are notebook pages relating to work I supervised in connection with the process used to form solid amorphous dispersions of a drug and hydroxypropylmethyl cellulose acetate succinate (or HPMCAS), as well as Examples 25 and 26 of the instant application. The notebook pages show that drugs were spray dried with HPMCAS to form solid amorphous dispersions. The dates on the notebook pages have been redacted. However, these examples were made prior to February 13, 1997.
7. I further declare that all statements made herein of my own knowledge are true and that all statements made on information are believed to be true; and further that these statements were made with the knowledge that willful false statements and the likes made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

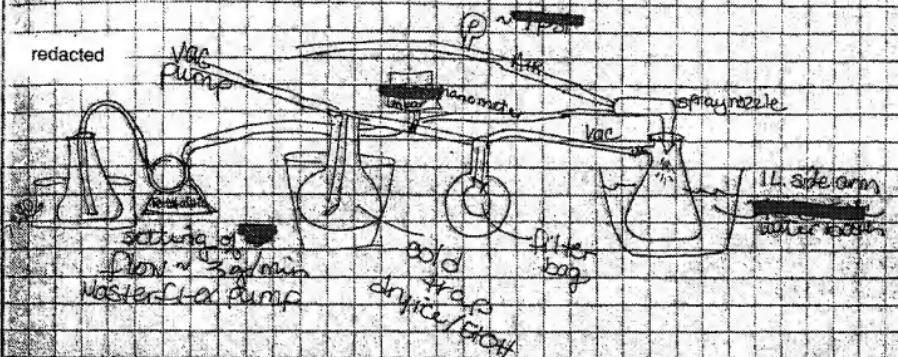
24 May 2007
Date



James A.S. Nightingale

GIBRI CorporateLegalPatentPC 9674 HPMCAS SDDoJASN Declaration 3-1-07.doc

From Page No. Making spray-dried solvent dispersion.
This is the set up.



Filter bag - paper folded rubber banded to inner part of the top

Masterflex pump - head 7013-20
tubing 6401-1C

base circ 16 CP-14386774 pages - see pg 15 for results

To Page No.

Witnessed & Understood by me.

Date,

Invented by

Date

Joel E. Becker

redacted

Reported by

John Hostetter

redacted

Project No. _____

Book No. _____

TITLE

73

From Page No. 6/13/ HPMCAS spray dried disp (: 10)
9

1800mg HPMCAS 200ml Acetone

200mg CMC

30°

Heated Acetone, added HPMCAS when no clumps, added CMC when

TDS = 3120 ppm redacted

H₂O = 45.55%

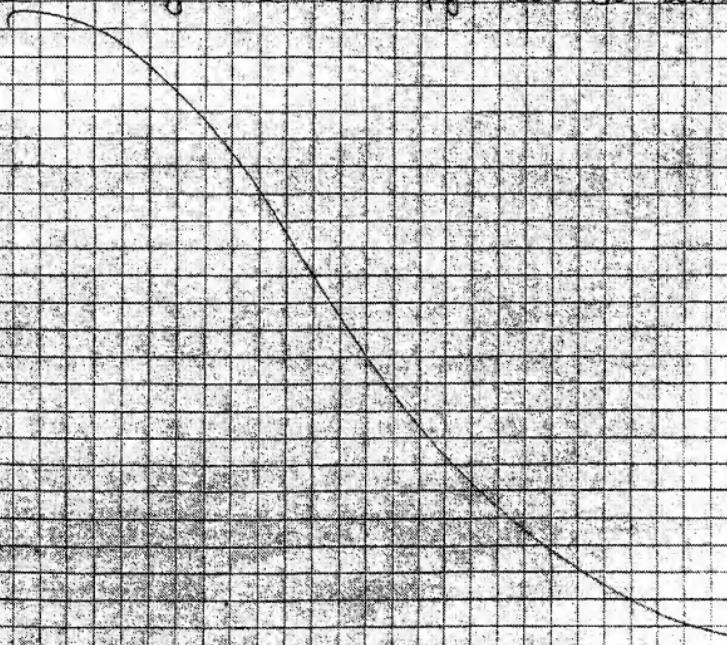
TFC = 440 mbar

pump setting = 3 (~3ml/min.)

air pressure = 10psi

and 6420 ppm

Tested C Day 1 - Data on pg 1330-83 looks good



To Page No.

Witnessed & Understood by me,

John E. Baile

Date

redacted

Invented by

redacted

Date

redacted

Project No. _____
Book No. 330

TITLE _____

From Page No. _____

See 1380-79

Satisfactory 1:2 & 1:5 Dispersion, 21 after vacuum drying overnight.

For 1:2 \Rightarrow 4.0 mg / 10 ml \Rightarrow 200 $\mu\text{g}/\text{ml}$
 1:5 \Rightarrow 10.02 mg / 10 ml \Rightarrow 200.2 $\mu\text{g}/\text{ml}$

Griseofulvin crystallization inhibition exp.										Sheet:	Date:	redacted	
										BRI Ref:	1350-68		
										Analyser:	C1/H ratio		
RECEPTOR SOLUTION: 10ml of 50% v/v H₂O/POPC-H₂O, pH 8.5,													
DRUG: Griseofulvin/HPMCAS spray-dried Dispersion													
2 theoretical flux, concentration: 200$\mu\text{g}/\text{ml}$													
Dissolution of (1:10) 10% Griseofulvin/HPMCAS spray-dried dispersion, Day 1													
HPLC ANALYSIS													
C18 column (Phenomenex, Ultrasorb)										Standard Factor:			
BNRD: 0.0204 NH₄PO₄, pH 3.0/AON										V-INT:	11.47532157	SLOPE:	17.3295123
A										B	Peak#1	C	Peak#2
(min)	4000	PPM	suc	min	4000	PPM	suc	min	4000	PPM	suc	min	4000
0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	223.47	94.388450	205.657202	0.4	205.177	101.075664	15.76523410	0.6	205.177	74.1557113	15.5444776	0.6	205.177
5	1485.17	173.250262	620.520005	5	1441.17	165.000000	365.943000	5	1441.17	165.000000	365.943000	5	1441.17
30	1521.05	174.315456	494.073864	30	1637.05	167.070445	487.071576	30	1637.05	162.210202	307.546391	30	1637.05
50	1218.45	174.023822	310.055203	50	1482.37	173.025547	1026.7552	50	1482.37	173.025547	1026.7552	50	1482.37
120	1464.01	175.295207	206.513203	120	1453.15	165.412184	2050.62723	120	1453.15	165.412184	2050.62723	120	1453.15
150	1455.42	175.295207	613.987205	150	1627.33	155.758965	3107.251506	150	1627.33	155.758965	3107.251506	150	1627.33
1200	1422.84	176.291187	381.624247	1200	1485.75	160.664427	2022.0156	1200	1485.75	160.664427	2022.0156	1200	1485.75
B										E	Peak#1	F	Peak#2
(min)	4000	PPM	suc	min	4000	PPM	suc	min	4000	PPM	suc	min	4000
0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	202.72	151.050165	25.455790	0.5	170.45	82.055468	20.17133665	0.5	170.45	82.055468	20.17133665	0.5	170.45
5	1420.21	183.02221	422.025157	5	1474.00	182.916132	385.703185	5	1474.00	182.916132	385.703185	5	1474.00
20	1457.25	180.020207	475.230779	20	1500.00	177.022035	481.020309	20	1500.00	177.022035	481.020309	20	1500.00
40	1485.75	173.316055	482.226000	40	1534.00	174.025547	1021.020308	40	1534.00	174.025547	1021.020308	40	1534.00
120	1420.82	163.422329	196.486912	120	1602.04	172.020003	2000.10633	120	1602.04	172.020003	2000.10633	120	1602.04
150	1489.00	171.295141	398.945311	150	1495.00	171.015653	3087.532063	150	1495.00	171.015653	3087.532063	150	1495.00
1200	807.03	91.2257856	194.0229131	1200	1120.01	120.020112	158427.111	1200	1120.01	120.020112	158427.111	1200	1120.01

0 30 60 90 120 150 180

Time (min)

● Task-1 ← Task-2 → Task-3 - filter-1 * filter-2 →

To Page No. _____

Witnessed & Understood by me,

Date

Invented by

Date

John D. Moran

redacted

Approved: John D. Moran AIA

redacted

TITLE

From Page No.

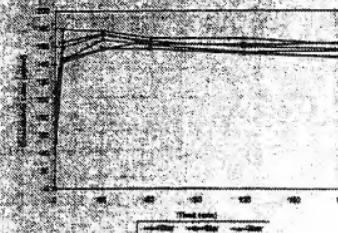
14 Crisprf/wvin/HPMCAS

500mg Ons 2250ml
20g HPMCAS 1/200ml

Time	min	air	140	160	Action	pump
12:350	0	11	352	538	45C	25
4:15	25	11	354	558	44C	25
4:40	50	11	383	512	312	25
5:00	70	11	300	562	58C	7.5

end - when I came back in the room I checked on the spray, the filter must have been plugged because the spray nozzle still had "popped" & wasn't sealing, but the vacuum was still reading 300mbar. There wasn't much liquid left to spray, so I turned off the feed pump, I let the dispersion dry as much as possible. When recovering the dispersion - it looked OK-not wet, I still vacuum-dried it overnight anyway.

To	[REDACTED]
Date	[REDACTED]
Reported by	[REDACTED]
Date Performed	redacted
Comments	[REDACTED]
Signature	[REDACTED]



To Page No.

Witnessed & Undersigned by me,

Date
[REDACTED]

Invented by

Redacted

Date
[REDACTED]